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EXAMINER	
EPPERSON, JON D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/879,279	DACE ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 32-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 32-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed February 16, 2007 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claim 11 was pending. Applicants added claims 32-51. Therefore, claims 11 and 32-51 are examined on the merits (e.g., see 2/16/07 Response, page 2, "all of new claims 32-51 are readable upon the elected species").

Withdrawn Objections/Rejections

4. All rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 103

5. Claims 11 and 32-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jakobsen et al. (US Pub. No. 2003/0077609 A1) (Priority to 60/278,598, filed on **March 25, 2001**) (of record) and Cregan et al. (Cregan, P.B.; Mudge, J.; Fickus, E.W.; Marek, L.F.; Danesh, D.; Denny, R.; Shoemaker, R.C.; Matthews, B.F.; Jarvik, T.; Young, N.D. "Targeted Isolation of Simple Sequence Repeat Markers through the use of Bacterial Artificial Chromosomes" *Theor.*

Appl. Genet. **1999**, *98*, 919-928) (of record) and Sambrook et al. (Sambrook J. and Russell, D.W. Molecular Cloning: A laboratory Manual. New York: Cold Spring Harbor Laboratory. **January 15, 2001**, Vol. 2, pages 1.1-1.29, 11.35 and 11.98-11.106) (of record, except for pages 1.1-1.29) and Brown (Brown, T.A. Genomes. New York: John Wiley & Sons, Inc. **1999**, pages 18-23 and 136-137) (of record) and Liu et al. (Liu et al. "Development of simple sequence repeat DNA markers and their integration into a barley linkage map" *Theor. Appl. Genet.* **1996**, *93*, 869-876).

For ***claims 11, 32, and 33***, Jakobsen et al. (see entire document) disclose methods for using modified "locked nucleic acids" (LNAs) for "the isolation, purification, amplification, detection, identification, quantification, or capture of nucleic acids" including applications in gene mapping and/or genotyping (e.g., see Jakobsen et al., abstract; see also page 4, paragraph 43, see also page 6, paragraph 63), which reads on the elected invention. For example, Jakobsen et al. disclose providing one or more modified oligonucleotide conjugates, wherein each of the modified oligonucleotide conjugates comprises at least one locked nucleic acid and a linking molecule (e.g., see Jakobsen et al., paragraph 14 wherein LNAs are disclosed; see also paragraph 49 wherein Applicants' elected "biotin" species is disclosed; see especially page 7, Example 2, see also paragraph 76; see also paragraphs 53-63). In addition, Jakobsen et al. disclose incubating a sample of nucleic acids with the modified oligonucleotide conjugates, thereby forming one or more hybridized duplexes (e.g., see Jakobsen et al., page 7, Example 2 wherein the "locked" modified oligonucleotide conjugates were used to "hybridize" to a sample of 5' biotin-labeled 50-mer or 30-mer oligonucleotide, each encompassing 1 to 5 SNPs [single nucleotide polymorphisms] for SNP genotyping; see

also page 6, paragraph 55, "In a further aspect, oligonucleotides of the invention may be used to construct new affinity pairs ... The affinity pairs may be used in ... capture and detection of a diversity of the target molecules"; see also paragraph 63, "Assay using an immobilized array of nucleic acid sequences may be used for determining the sequence of an unknown nucleic acid; single nucleotide polymorphism (SNP) analysis; analysis of gene expression patterns from a particular species, tissue, cell type, etc.; gene identification"). Jakobsen et al. further disclose contacting substantially all of the hybridized duplexes with a linking source, such that the linking molecule of each duplex that contacts the linking source forms a bond with the linking source (e.g., see page 7, Example 2, especially paragraph 76 wherein Applicants' elected "streptavidin" species is disclosed). Finally, Jakobsen et al. disclose separating substantially all of the hybridized duplexes from the sample of nucleic acids (e.g., see page 7, Example 2, especially washing steps).

For ***claim 44***, Jakobsen et al. disclose complementary sequences (e.g., see Jakobsen et al., page 1, paragraph 11; see also page 7, Example 2, paragraph 75).

For ***claim 45***, Jakobsen et al. disclose biotin bound to 5' end (e.g., page 7, Example 2, paragraph 76; see also page 3, column 1, paragraph 28; see also page 5, paragraph, column 1, paragraph 49).

For ***claim 46***, Jakobsen et al. disclose biotin (e.g., see page 7, Example 2, paragraph 76).

The prior art teachings of Jakobsen et al. differ from the claimed invention as follows:

For ***claims 11, 32, and 33***, Jakobsen et al. fail to recite the use of "simple sequence repeat" (SSR) target molecules. Although, Jakobsen et al. teach the use of target molecules like SNPs as physical markers in gene mapping and/or genotyping experiments (e.g., see page 7, Example 2; see also page 6, paragraph 63), Jakobsen et al. fail to explicitly refer to other types of physical markers like SSR target molecules. In addition, Jakobsen et al. fail to expressly state, with regard to claim 11 (not claim 32), that they use a target simple sequence repeat portion wherein the simple sequence repeat portion of the hybridized duplex is a portion of an insert in a 3.5 kb clone.

For ***claim 34***, Jakobsen et al. fail to disclose simple sequence repeat portions comprising 1, 2, 3, or 4 base repeats.

For ***claims 35-37***, Jakobsen et al. fail to teach the use of alkaline buffer for the dissociation of the target molecule in the range of pH 9-10.

For ***claim 38***, Jakobsen et al. fail to teach the use of a strand displacing "A" helix.

For ***claim 39***, Jakobsen et al. fail to teach the formation of a new library that is enriched in the targeted SSRs.

For ***claims 40-43***, Jakobsen et al. fail to teach double stranded circular DNA plasmid libraries.

For ***claim 45***, Jakobsen et al. disclose biotin bound to 5' end (e.g., page 7, Example 2, paragraph 76; see also page 3, column 1, paragraph 28; see also page 5, paragraph, column 1, paragraph 49).

For ***claim 47***, Jakobsen et al. fail to teach streptavidin-coated beads.

For ***claim 48***, Jakobsen et al. disclose streptavidin (e.g., see page 7, Example 2,

paragraph 76).

For ***claim 49***, Jakobsen et al. fail to teach the use of a magnet.

For ***claim 50***, Jakobsen et al. fail to teach the use of streptavidin-coated magnetic beads, incubating at pH of around 9.5 for dissociation, transforming the simple sequences into *E. coli* and sequencing the repeats.

For ***claim 51***, Jakobsen et al. fail to teach the use of a target simple sequence repeat that is 5'-$(CA)_6$-3' wherein the modified oligonucleotide conjugate comprises 3 biotinylated $(GT)_6$-5' bicyclic structures, wherein the LNAs occur on at least the first G. However, Jakobsen et al. do disclose the use of biotin (see above) and bicyclic LNAs (e.g., see Jakobsen et al., paragraphs 14 and 29).

However, the combined references of Cregan et al. Sambrook et al., Brown, and Liu et al. teach the following limitations that are deficient in Jakobsen et al.:

For ***claims 11, 32, 33, 44***, the combined references of Cregan et al., Sambrook et al., Brown, and Liu et al. (see entire documents) teach the use of SSRs as target molecules (e.g., see Cregan et al., abstract; see also Brown, page 136, "Mini- and microsatellites" section). Furthermore, the use of "extraction" techniques including the application of streptavidin-coated magnetic beads is also taught (e.g., see Sambrook et al., page 11.99, figure 11-20). The combined references of Cregan et al., Sambrook et al., Liu et al., and Brown also teach the use of SSR portion comprising 1, 2, 3, or 4 base repeats (e.g., see Brown, page 136, column 2, last paragraph wherein CACACACACACACACA is exemplified i.e., a "2 base repeat"; see also Cregan et al., page 919, column 2, last paragraph wherein CA, ATT and ATGT are disclosed i.e., 2, 3

and 4 base repeats).

In addition, the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown teach the use of a 3.5 kb clone (e.g., see Sambrook et al., page 1.16, bottom paragraph disclosing that smaller plasmids are more durable; see also page 1.19, paragraph 1 showing that the small plasmids are less expensive and easier to purify; see especially, top of page 1.26, "Plasmids ranging in size from 2.6 kb to 85 kb can be introduced ... " showing that plasmids of a 3.5 kb size were routinely used in the art). In addition, the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown teach that plasmid clones can be used to produce clones of simple sequence repeats (e.g., see Liu et al., page 870, column 1, Materials and Methods).

Alternatively, the Examiner contends that the phrase "wherein the simple sequence repeat portion of the hybridized duplex is a portion of an insert in a 3.5 kb clone should not be afforded any patentable weight because it represents intended use of a product-by-process limitation that does not materially change the structure of the simple sequence repeat. See MPEP § 2113, "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." Here, the "portion" of the clone could consist only of the "insert" and not the "plasmid" (see specification, page 13, line 11), which would not afford any structural

difference for the simple sequent repeat. Thus, the process limitation (i.e., making the simple sequence repeat from a 3.5 kb clone) does not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill would expect the product (i.e., the insert) to be the same no matter how it was synthesized and/or prepared.

For ***claims 35-37***, the combined references of Cregan et al., Sambrook et al., Brown and Liu et al. teach the use of alkaline buffer to dissociate the target molecules (e.g., see page 11.104, step 13 a-b). The combined references do not explicitly teach the use of pH = 9-10, but they do teach the addition of a strong base (i.e., 0.1 M NaOH, pH = 13), which would be expected to produce pH ranges between 9-10 when combined with other more acidic components (e.g., the sample and/or sample buffer i.e., pH < 9-10). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

For ***claim 38***, the combined references of Cregan et al., Sambrook et al., Brown and Liu et al. do not explicitly state that a strand displacing "A" helix is formed but the Examiner contends that this would be an inherent disclosure because use of the same CACACACACACA target is disclosed (e.g., compare Brown, page 136, column 2, last

paragraph to Applicants' 131 declaration, File TNC01_E04.21, bases underlined from 221-232).

For ***claim 39***, the combined references of Cregan et al., Sambrook et al., Brown, and Liu et al. teach the formation of a new library enriched in SSRs (e.g., see Cregan et al., page 921, middle paragraph, "Selected colonies were picked onto microtiter plates followed by two additional cycles of screening and purification"; see also Sambrook et al., page 11.98, paragraphs 2-3).

For ***claims 40-43***, the combined references of Cregan et al., Sambrook et al., Brown, and Liu et al. teach double stranded circular DNA plasmid libraries (e.g., see Cregan et al., page 921, middle paragraph; see also Sambrook et al., figure 11-20).

For ***claim 47***, the combined references of Cregan et al., Sambrook et al., Brown, and Liu et al. teach streptavidin-coated beads (e.g., see Sambrook et al., page 11.99, figure 11-20).

For ***claim 49***, the combined references of Cregan et al., Sambrook et al., Brown, and Liu et al. teach the use of streptavidin-coated paramagnetic beads (e.g., see Sambrook et al., page 11.99, figure 11-20).

For ***claim 50***, the combined references of Cregan et al., Sambrook et al., Brown, and Liu et al. teach the use of streptavidin-coated magnetic beads (e.g., see Sambrook et al., page 11.99, figure 11-20), incubating at pH of around 9.5 for dissociation (see section for ***claims 4-6*** above), transforming the simple sequences into *E. coli* (e.g., see Cregan et al., page 921, paragraph 1) and sequencing the repeats (e.g., see Cregan et al., page 921, last paragraph).

For ***claim 51***, the combined references of Cregan et al., Sambrook et al., Brown, an Liu et al. teach the same is 5'-$(CA)_6$-3' target, which would render obvious the 3 biotinylated $(GT)_6$-5' bicyclic structures because Jakobsen et al. teach the use of "complimentary" structures (see above), which would include $(GT)_6$ because it is complementary to $(CA)_6$ and as noted above the combined references teach biotin and the use of bicyclic LNAs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to capture "simple sequence repeats" (SSRs) as taught by the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown using "locked nucleic acids" (LNAs) as taught by Jakobsen et al. because Jakobsen et al. teach that LNAs possess enhanced specificity/affinity for target sequences and thus can be used to improve all hybridization reactions and specifically point to the PCR based characterization of physical markers commonly used in gene mapping and/or genotyping experiments (e.g., see Jakobsen et al., page 6, paragraph 63; see especially page 7, Example 2), which would encompass the physical markers exemplified by the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown (i.e., the references represent analogous art because "simple sequence repeats" (SSR) and "single nucleotide polymorphisms" (SNP) markers are both PCR-based, co-dominant and abundant molecular markers from eukaryotic genomes that are being widely used in genetic mapping, phylogenetic studies and marker-assisted selection) (e.g., see Brown, pages 18-22 for background information on the use of SNPs and SSRs). In addition, Cregan et al. state that the bacterial artificial chromosomes (BACs) used to isolate SSR markers "can

readily be extended to other types of DNA markers, including single nucleotide polymorphisms [i.e., SNPs]" (e.g., see Cregan et al., page 919, column 2, paragraph 1), which would encompass the SNPs disclosed by Jakobsen et al. A person of skill in the art would have been motivated to use the LNAs to search for SSRs because Cregan et al. state that LNAs provide "enhanced hybridization and [PCR] priming properties" (e.g., see Cregan et al., page 1, paragraph 10; see also page 1, paragraph 11 wherein beneficial PCR results are also disclosed), which would increase the efficiency of searching for the SSRs (just as they do for SNPs) because the SSRs represent PCR-based markers that require hybridization and PCR priming (e.g., see Cregan et al., page 919, column 2, last paragraph). Furthermore, SSRs represent a "preferred embodiment" of physical markers for gene mapping and/or genotyping (e.g., see Cregan et al., page 919, column 2, last paragraph, "The high level of informativeness and co-dominance of microsatellite markers, their widespread occurrence in eukaryotic genomes, and easy amplification via standard PCR technology, make SSR the current marker of choice [i.e., a preferred embodiment] in many species"; see also Brown, page 21, column 1, "Microsatellites [SSRs] are more popular ... [because they] are more conveniently spaced through the genome. Second, the quickest way to type a length polymorphism is by PCR, but PCR typing is much quicker and more accurate with sequences less than 300 bp in length [i.e., SSRs]; see also page 21, column 2, wherein the drawbacks of SNPs are outlines e.g., they have only two alleles; see also pages 136-137, "Mini- and microsatellites" section). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Cregan et al. state that their BAC technology will work with both

SNPs and SSRs and Sambrook et al. state that their streptavidin-coated magnetic beads are particularly well suited for selecting large genomic DNA clones using BACs (see Cregan et al., page 919, column 2, paragraph 1, "This targeted approach to identifying new DNA markers [i.e., SSRs] can readily be extended to ... single nucleotide polymorphisms"; see also Sambrook et al., page 11.98-11.100, especially figure 11-20).

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art to use a plasmid that is 3.5 kb in length to screen for the simple sequence repeats because Liu et al., for example, explicitly state that plasmids can be used for this purpose (e.g., see Liu et al., page 870, Materials and Methods, "The procedures for constructing a small-insert plasmid library and for screening of the SSR-containing clones were as previously described"). In addition, a person of ordinary skill in the art would have been motivated to use plasmids because they are cheap, stable, easy to use via facile PCR and molecular biology techniques, easy to purify, and can be used to produce, screen and sequence a library (e.g., see Liu et al., page 870, column 1, Materials and Methods; see also Brown, page 21, column 1, paragraph 1; see also Sambrook et al., page 1.16, bottom paragraph disclosing that smaller plasmids are more durable; see also page 1.19, paragraph 1 showing that the small plasmids are less expensive and easier to purify; see especially, top of page 1.26, "Plasmids ranging in size from 2.6 kb to 85 kb can be introduced ... " showing that plasmids of a 3.5 kb size were routinely used in the art). Finally, a person of ordinary skill in the art would have reasonably expected to be successful because molecular cloning techniques using plasmids were routinely practiced in the art even with Applicants' claimed simple sequence repeats (e.g., see Sambrook et

al., pages 1.1-1.29; see also Liu et al., Materials and Methods).

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims (e.g., claims 32-51) and/or arguments.

[1] Applicants argue, "In response to the above-discussed rejection of claim 11 based on 35 U.S.C. § 103(a), applicants respectfully submit the attached Declaration under 37 CFR § 1.131 as Exhibit A ... The Examiner first contended in the final Official Action mailed April 7, 2005 that the 35 C.F.R. § 1.131 Declaration submitted November 17, 2004 with Amendment A was defective. In response, applicants submitted a replacement 37 C.F.R. § 1.131 Declaration with Amendment B, filed October 7, 2006. In an Advisory Action dated November 29, 2006, the Patent Office refused to accept the 37 C.F.R. § 1.131 Declaration submitted with Amendment B, presumably because the patent application was under final rejection. Accordingly, applicants resubmit herewith the 37 C.F.R. § 1.131 Declaration filed with Amendment B."

[1] As an initial matter the Examiner notes that no § 1.131 Declaration was "attached" with the present office action. However, Applicants stated that the alleged "attached" copy is just a "resubmission" of the copy that was filed on October 7, 2006. Thus, all reference to a § 1.131 Declaration will refer to the October 7, 2006 submission.

[2] Applicants argue, "the [present] 37 CFR § 1.131 Declaration addresses all of the Patent Office's assertions of defectiveness ... Specifically, applicants respectfully submit that the 37 C.F.R. § 1.131 Declaration includes signatures from both inventors" (e.g., see 2/16/07 Response, page 3, paragraphs 1 and 2).

[2] The Declaration filed on October 7, 2006 under 37 CFR § 1.131 has been considered but is ineffective to overcome the 35 U.S.C. § 103(a) reference.

[2] The declaration is defective because it does not contain a signature from all of the inventors as required by MPEP § 715.04. Although, Applicants state that "both" signatures have been provided such is not the case. The signature for William Kimmerly is still missing (e.g., see 10/7/05 Declaration, page 4). Thus, all of Applicants' arguments on pages 3-5 are moot. However, in an attempt to further prosecution the following responses are noted below.

[3] Applicants argue, "The declaration also states that the inventive activity occurred in the United States" (e.g., see 2/16/07 Response, page 3, paragraph 2).

[3] The Declaration reads, "The subject matter embodied in claims 1-8, 11-15, 18-24 and 31 ... was invented ... in the United States" (e.g., see 10/11/05 Declaration, page 2, paragraph 4). Thus, Applicants have not made an averment for newly added claims 32-51 and thus the declaration is again defective with respect to these claims (i.e., the requirement is only satisfied for claim 11).

[4] Applicants argue, "the Declaration sets forth additional facts and/or evidence to corroborate completion of the invention before the particular date ... Exhibit A ... records

experimental conditions related to capturing specific target nucleotide sequences ... Specifically, the first page of Exhibit A describes ... 'Torrey-2' ... $(GC)_6$, with the LNA residues ... shown in bold ... [and the linking molecule] biotin. The second page of Exhibit A ... records further experimental conditions ... related to capturing specific target nucleotide sequences ... wherein each duplex [formed] comprises a target simple sequence repeat ... and an LNA conjugate ... [wherein a] tomato library DNA was incubated with [said] Torrey-2 LNA ... the third page of Exhibit A ... describes the protocol used ... [including the use of] streptavidin-coated magnetic beads ... ethanol precipitation ... DH12S cells ... Further Exhibit B is a true and accurate reproduction of the results of sequence data chromatographs resulting from the experiments discussed above and provide[d] in Exhibit A ... Exhibit B verifies that SSRs were recovered and that the experiment was successful" (e.g., see 2/16/07 Response, pages 3 and 4).

[4] The affidavit of declaration must state facts and produce such documentary evidence and exhibit in support thereof as are available to show conception and completion of invention in this country, at least conception being at a date prior to the effective date of the references. See MPEP 715.07 and 715.07(c). A general allegation that the invention was completed prior to the date of the reference is not sufficient. *Ex parte Saunders*, 1883 C.D. 23, 23 O.G. 1223 (Comm'r Pat. 1883). Similarly, a declaration by the inventor to the effect that his or her invention was conceived or reduced to practice prior to the reference date, without a statement of facts demonstrating the correctness of his conclusion, is insufficient to satisfy 37 CFR 1.131. See MPEP 715.07. 37 CFR 1.131(b) requires that original exhibits of drawings or records, or photocopies thereof, accompany and form part of the affidavit or declaration or their absence satisfactorily explained. Se MPEP 715.07. Here, Applicants fail to set forth any evidence

concerning the use of the claimed 3.5 kb clone. In addition, no "separation" steps have been set forth. Although page 147 of the laboratory notebook stated that "something" worked it is unclear what actually did work. Furthermore, Applicants make no claim in the Declaration that the results set forth in Exhibit B were actually obtained before the March 25, 2001 date. That is, Applicants only state that the subject matter set forth in Exhibit A occurs before the March 25, 2001 date (e.g., see Declaration, page 2, paragraph 5). Thus, whether the protocol set forth on page 150 was actually carried out to completion before the March 25, 2001 date is unclear.

[5] Applicants argue, "the Declaration and data provided in Exhibits A and B are commensurate in scope with the pending claims. Under MPEP § 715.03, a cited reference applied against generic claims may be antedated by a declaration under 37 C.F.R. § 1.131 showing completion of the invention of only a single species within the genus prior to the effective date of the reference" (e.g., see 2/16/07 Response, paragraph bridging pages 4 and 5).

[5] The Examiner respectfully disagrees. "It appears to be well settled that a single species can rarely, if ever, afford support for a generic claim." *In re Clarke*, 356 F.2d 987, 961, 148 USPQ 665, 670 (CCPA 1966), citing *In re Soll*, 97 F.2d 623, 38 USPQ 189 (CCPA 1938); *In re Wahlforss*, 117 F.21 270, 48 USPQ 397 (CCPA 1941). While the courts do not "fix any definite number of species which will establish completion of a generic invention ... in the case of a small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably large number of reductions to practice would probably be necessary." *Id.* Thus, even in a well-defined and highly predictable genus like the

halogens, the courts still require more than one species. Here, Applicants' claim 11 would encompass virtually an unlimited number of species because it does not place any restriction on the number of atoms, types of atoms or means in which said atoms are connected to form the multitude of oligonucltoide conjugates, locked nucleic acids, linking molecules, linking source, etc. Therefore, Applicants disclosure of Torrey-2 linked to biotin does not provide adequate support for this broad genus.

[6] Applicants argue, "a 37 C.F.R. § 131 declaration need only show prior invention of so much of the claimed subject matter as is disclosed by the reference" and cite *In re Stempel* in support of this position. (e.g., see 2/16/07 Response, page 5, paragraphs 1 and 2).

[6] A reference which discloses several species of a claimed genus can be overcome directly under 37 CFR 1.131 only by a showing that the applicant completed, prior to the date of the reference or activity, all of the species shown in the reference. *In re Stempel*, 241 F.2d 755, 113 USPQ 77 (CCPA 1957). Here, Applicants' declaration provides support for only Torrey-2-linked to biotin for use in conjunction with a tomato library, which does not show completion of the many species disclosed in Jakobsen. For example, the 131 declaration fails to disclose other species of linking molecule (other than biotin) such as digoxigenin (e.g., see Jackobsen, paragraph 49) that can bind to substrate bound antibodies. In addition, the 131 declaration fails to set forth many of the species of locked nucleic acids set forth in Jackobsen including both "bicyclic" and "tricyclic" RNA analogs. The 131 declaration only sets forth one type of locked nucleic acid for DNA. Therefore, Applicants' 131 declaration fails the test set forth in *In re Stempel*.

[7] Applicants argue, "none of the remaining references ... suggest all the claim limitations of claim 11 ... therefore ... the 35 U.S.C. § 103(a) rejection ... [should be] withdrawn" (e.g., see 2/16/07 Response, page 5, last two paragraphs).

[7] The Jakobsen reference has not been removed for the reasons outlined above and, as a result, Applicants' arguments are moot.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

New Rejections

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 32-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claim 32** recites the limitation "the captured simple sequence repeat portion" in line 1. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 32 and all dependent claims are rejected under 35 USC 112, second paragraph.

B. **Claim 50** recites the limitation "the hybridization duplexes" in line 12. There is insufficient antecedent basis for this limitation in the claim. The Examiner recommends

"the hybridized duplexes" as a replacement. Therefore, claim 50 and all dependent claims are rejected under 35 USC 112, second paragraph.

C. **Claim 51** recites the limitation "the LNAs" in line 3. There is insufficient antecedent basis for this limitation in the claim. The Examiner recommends "the at least one locked nucleic acid" as a replacement. Therefore, claim 51 and all dependent claims are rejected under 35 USC 112, second paragraph.

D. **Claim 51** recites the limitation "the target source" in line 4. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 51 and all dependent claims are rejected under 35 USC 112, second paragraph.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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Jon D. Epperson, Ph.D.
May 9, 2007

JON EPPERSON
PRIMARY EXAMINER